

Amendments to the Specification

Please replace paragraph [0052] with the following paragraph:

[0052] For example, octapeptides (P₄-P'₄) for MMP 2 and MMP 9

have been identified (see Table 1), which octapeptides simulate the cleavage sequence of the collagen chain and are cleaved with particular efficiency by MMP 2 and 9 (in what follows, amino acids are abbreviated in accordance with the international three-letter code):

Please replace paragraph [0054] with the following:

[0054] Furthermore, in the case of cathepsin B, substrate-specific peptides are

Table 1:

Peptide	P ₄	P ₃	P ₂	P ₁	P' ₁	P' ₂	P' ₃	P' ₄
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Gly-Pro-Leu-Gly-Ile-Ala-Gly-Gln [SEQ. ID No. 1]

Gly-Pro-Gln-Gly-Ile-Trp-Gly-Gln [SEQ. ID No. 2]

(Netzel-Arnett et al., *Biochemistry* 32, 1993, 6427-6432)

known with the sequence:

-Gly-Phe-Leu-Gly- SEQ. ID No. 3

-Gly-Phe-Ala-Leu- SEQ. ID No. 4

-Ala-Leu-Ala-Leu- SEQ ID No. 5

-Arg-Arg- or -Phe-Lys- SEQ ID No. 6

Werle, B., Ebert, E., Klein, W., and Spiess, E. (1995), *Biol. Chem. Hoppe-Seyler* 376, 157-164; Ulrich, B., Spiess, E., Schwartz-Albiez, R., and Ebert, W. (1995), *Biol. Chem. Hoppe-Seyler* 376, 404-414).

Please replace paragraph [0055] as follows:

[0055] The peptide sequence that contains intended peptide cleavage points relevant for the target enzyme can also be constructed such that the intended peptide cleavage point is repeated a plurality of times, for example by:

-Gly-Pro-Leu-Gly--Ile-Ala-Gly-Gln-Gly-Pro-Leu-Gly--Ile-Ala-Gly-Gln **SEQ ID No. 7**

or

-Phe-Lys-Phe-Lys-Phe-Lys-Phe-Lys-Phe-Lys- **SEQ. ID No. 8**

or a repetitive peptide sequence can be integrated that increases the distance between the thiol-binding group and the relevant intended peptide cleavage point, as for example by:

-(Gly)_n-Phe-Lys-Phe-Lys-

with, preferably, n = 2 to 20, more preferably n ≤ 12.

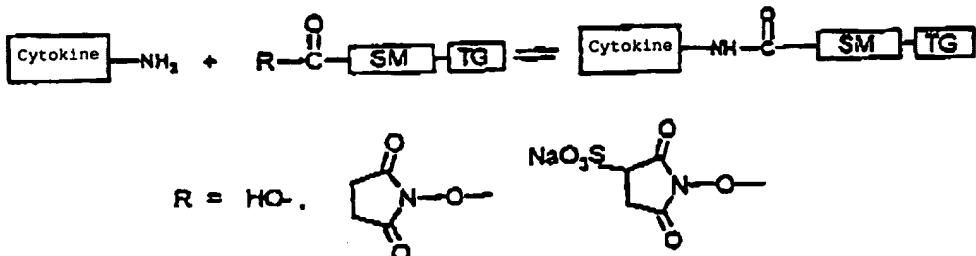
Please replace paragraph [0084] as follows:

[0084] Here the octapeptide

Gln-Gly-Ala-Ile-Gly-Leu-Pro-Gly **SEQ. ID NO. 9**

derivatized with maleimidoglycine 1 (Mr 848, prepared by solid-phase synthesis by Bachem AG, Switzerland) was reacted with doxorubicin according to the following method:

At the Examiner's request, Applicant is supplying a clear copy of the structure at the top of page 25 (attached at end of this paper).



for example, by reacting the cytokine with a spacer molecule containing a thiol-binding group, which spacer molecule exhibits a carboxylic acid or an activated carboxylic acid:

[0058] If the spacer molecule exhibits an N-hydroxysuccinimide ester group (N-hydroxysuccinimide or N-hydroxysuccinimide-3-sulfonic acid sodium salt), it is reacted directly with the cytokine. The reaction of the cytokine with a spacer molecule containing a thiol-binding group, which spacer molecule exhibits a carboxylic acid, to the corresponding thiol-binding derivatives takes place in the presence of a condensation agent, such as for example N,N'-dicyclohexylcarbodiimide (DCC) or N-cyclohexyl-N'-(2-morpholinoethyl)-carbodiimide methyl-*p*-toluene sulfonate (CMC), and if appropriate with the addition of N-hydroxysuccinimide or N-hydroxysuccinimide-3-sulfonic acid sodium salt. As a rule, the cytokines derivatized in this way are purified with the aid of gel chromatography. The above-described reactions are well known to a person skilled in the art (see, e.g., *Bioconjugate Techniques*, G. T. Hermanson, Academic Press, 1996).

[0059] The above-described drugs or drug derivatives are coupled to a carrier containing a polypeptide sequence with one or a plurality of cysteine groups, such as for example native or